

UNITED STATES PATENT AND TRADEMARK OFFICE  
CERTIFICATE OF CORRECTION

PAGE 1 of 2

PATENT NO.: 7,705,045  
APPLICATION NO.: 10/534,777  
ISSUE DATE: April 27, 2010  
INVENTOR(S): De Groot *et al.*

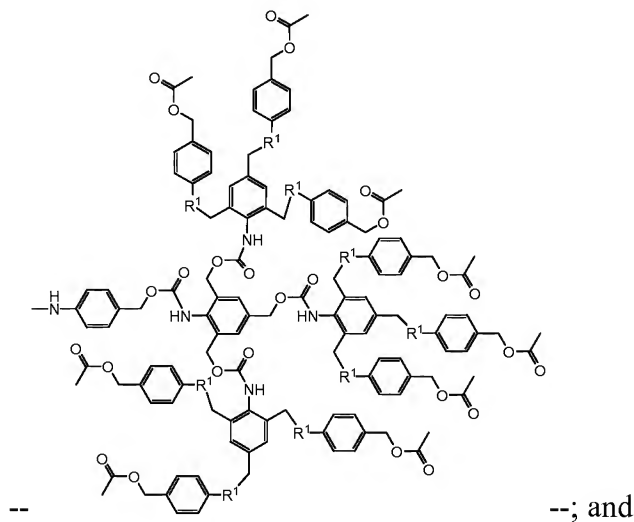
It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In claim 1, at column 127, line 27, delete “ $C(R^2)(R^3)Q-(W-)_w(X-)_x$ ” and replace with  $--C(R^2)(R^3)Q-(W-)_w(X-)_x--$ .

In claim 3, at column 128, line 45, delete “ $B=O$ ” and replace with  $--B = O--$ ; at column 128, line 47, delete “ $B=N$ ” and replace with  $--B = N--$ ; and at column 128, line 50, delete “ $B=O$ ” and replace with  $--B = O--$ .

In claim 4, at column 128, line 52, delete “ $B=O$ ” and replace with  $--B = O--$ .

In claim 7, at columns 147-148, insert



at column 161, line 49, delete “ $R^1=OC(O)O$ ” and replace with  $--R^1 = OC(O)O--$ .

In claim 16, at column 163, line 46, delete “ $B=O$ ” and replace with  $--B = O--$ ; at column 163, line 48, delete “ $B=N$ ” and replace with  $--B = N--$ ; and at column 163, line 51, delete “ $B=O$ ” and replace with  $--B = O--$ .

In claim 17, at column 163, line 53, delete “ $B=O$ ” and replace with  $--B = O--$ .

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It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In claim 31, at column 201, line 23, delete “R<sup>7</sup>=OC(O)O” and replace with  
--R<sup>7</sup> = OC(O)O--.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTORS: De Groot *et al.*

APPLICATION NO.: 10/534,777

PATENT NO.: 7,705,045

FILING DATE.: December 20, 2005

ISSUE DATE: April 27, 2010

TITLE: PRODRUGS BUILT AS MULTIPLE SELF-ELIMINATION-RELEASE SPACERS

ATTN: Certificate of Correction Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**REQUEST FOR CERTIFICATE OF CORRECTION UNDER 35 U.S.C. § 254**  
**AND 37 C.F.R. 1.322**

Sir:

Applicants hereby request that a Certificate of Correction be issued for U.S. Patent No. 7,705,045 pursuant to 35 U.S.C. § 254 and 37 C.F.R. 1.322.

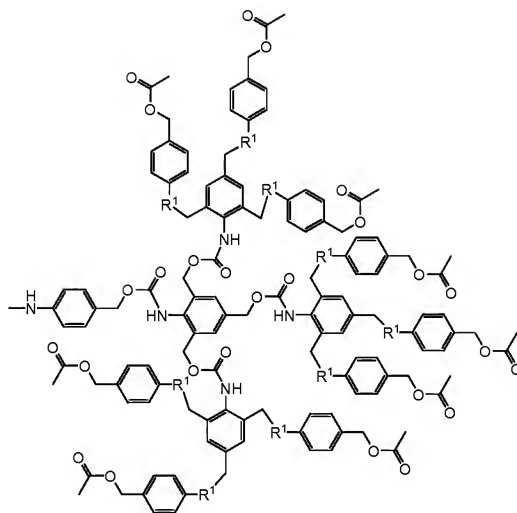
Applicants respectfully request that the corrections which appear on the enclosed Certificate of Correction issue. More specifically, Applicants submit that the following errors require correction:

1) claim 1, at col. 127, line 27, reads “C(R<sup>2</sup>)(R<sup>3</sup>)Q-(W-)<sub>w(X-x)</sub>” rather than “C(R<sup>2</sup>)(R<sup>3</sup>)Q-(W-)<sub>w(X-x)</sub>” as presented by Applicants in claim 4 (renumbered as claim 1 in the issued patent) at page 3 in the Amendment and Response dated December 1, 2009;

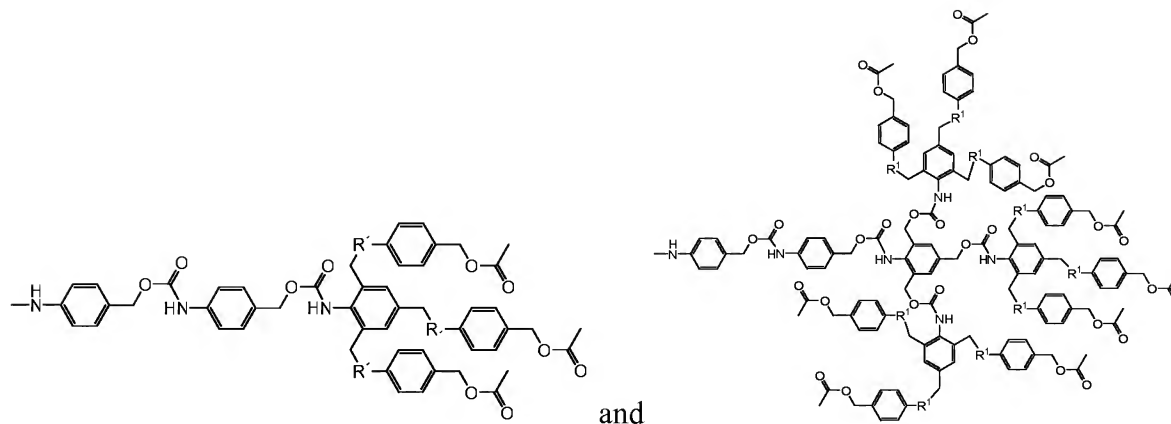
2) claim 3, at col. 128, lines 45, 47, and 50, reads “B=O”, “B=N”, and “B=O”, hence resembling a double bond rather than an equal sign in “B = O”, “B = N”, and “B = O” as presented by Applicants in claim 8 (renumbered as claim 3 in the issued patent) at page 5 in the Amendment and Response dated December 1, 2009;

3) claim 4, at col. 128, line 52, reads “B=O” and hence resembling a double bond rather than an equal sign in “B = O” as presented by Applicants in claim 9 (renumbered as claim 4 in the issued patent) at page 5 in the Amendment and Response dated December 1, 2009;

4) claim 7, at col.147-148, erroneously omits the structure:



which was presented between the structures:



in claim 14 (renumbered as claim 7 in the issued patent) at page 10, last line, left, in the Amendment and Response dated December 1, 2009;

5) claim 7, at col. 161, line 49, reads " $R^1=OC(O)O$ " and hence resembling a double bond rather than an equal sign in " $R^1 = OC(O)O$ " as presented by Applicants in claim 14 (renumbered as claim 7 in the issued patent) at page 13 in the Amendment and Response dated December 1, 2009;

6) claim 16, at col. 163, lines 46, 48, and 51, reads " $B=O$ ", " $B=N$ ", and " $B=O$ " hence resembling a double bond rather than an equal sign in " $B = O$ ", " $B = N$ ", and " $B = O$ " as presented by Applicants in claim 23 (renumbered as claim 16 in the issued patent) at page 16 in the Amendment and Response dated December 1, 2009;

7) claim 17, at col. 163, line 53, reads " $B=O$ " and hence resembling a double bond rather than an equal sign in " $B = O$ " as presented by Applicants in claim 24 (renumbered as claim 17 in the issued patent) at page 16 in the Amendment and Response dated December 1, 2009; and

8) claim 31, at col. 201, line 23, reads “ $R^7=OC(O)O$ ” and hence resembling a double bond rather than an equal sign in “ $R^7 = OC(O)O$ ” as presented by Applicants in claim 43 (renumbered as claim 7 in the issued patent) at page 24 in the Amendment and Response dated December 1, 2009.

For the convenience of the USPTO, a copy of the relevant pages of the Amendment and Response dated December 1, 2009, including claims 4, 8, 9, 14, 23, 24, and 43 (corresponding to claims 1, 3, 4, 7, 16, 17, and 31, respectively) are attached as “Exhibit A.”

Applicants believe no fee is necessitated by this Request for a Certificate of Correction as the errors apparently arose due to mistakes by the Patent Office. Nevertheless, if a fee is required for this submission, the Director is authorized to charge Attorney’s Deposit Account No. 50-1721. The USPTO is invited to call the undersigned attorney with any questions concerning submission of this paper.

Respectfully submitted,

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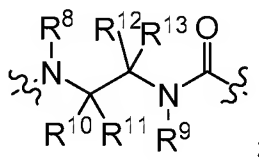
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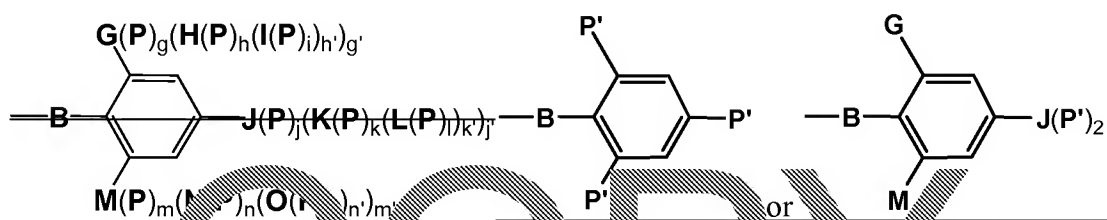
# EXHIBIT A

**Q** is  $-\text{O}-\text{CO}-$ ;

**A** is an  $\omega$ -amino aminocarbonyl cyclization elimination spacer having the formula:



each of **C**, **D**, **E**, and **F** independently is a self-eliminating multiple release spacer or spacer system and has the formula:



wherein

**B** is selected from NH, O, and S;

$[[\text{P}]]\underline{\text{P}}$  is  $\text{C}(\text{R}^2)(\text{R}^3)\text{Q}-(\text{W})_w(\text{X})_x$ ; wherein

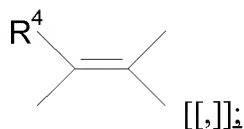
**Q** is  $-\text{O}-\text{CO}-$ ; and

**W** and **X** are as defined above;

**G**, **J**, and **M** independently are **P**, and  $g, h, i, h', g', j, k, l, k', j', m, n, o, m',$  and  $n'$  all equal 0; or

**G** and **M** are hydrogen $[[,]]$ ; and  $g, h, i, h', g', m, n, o, n',$  and  $m'$  all equal 0;

**J** is



and  $j=2$  and  $j'=0$ ;

(S(=O)R<sub>x</sub>), phosphonoxy (OP(=O)(OH)<sub>2</sub>), and phosphate (OP(=O)(OR<sub>x</sub>)<sub>2</sub>),  
wherein R<sub>x</sub>, R<sub>x</sub><sup>1</sup> and R<sub>x</sub><sup>2</sup> independently are selected from a C<sub>1-6</sub> alkyl group, a C<sub>3-20</sub> heterocyclyl group and a C<sub>5-20</sub> aryl group; or

alternatively, two or more of R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup>, and R<sup>13</sup> are connected to one another to form one or more aliphatic or aromatic cyclic structures;

each **Z** is independently a therapeutic or diagnostic moiety;

a is 0 or 1;

c, d, e, and f are independently an integer from 2 (included) to 24 (included);

w and x are independently an integer from 0 (included) to 5 (included); and

n is an integer of 0 (included) to 10 (included).

5-6. (Canceled)

7. (Previously presented) The compound according to claim 4, wherein the **Z** groups are linked to the self-eliminating multiple release spacer or spacer system via an O, S, or aromatic N of the **Z** group.

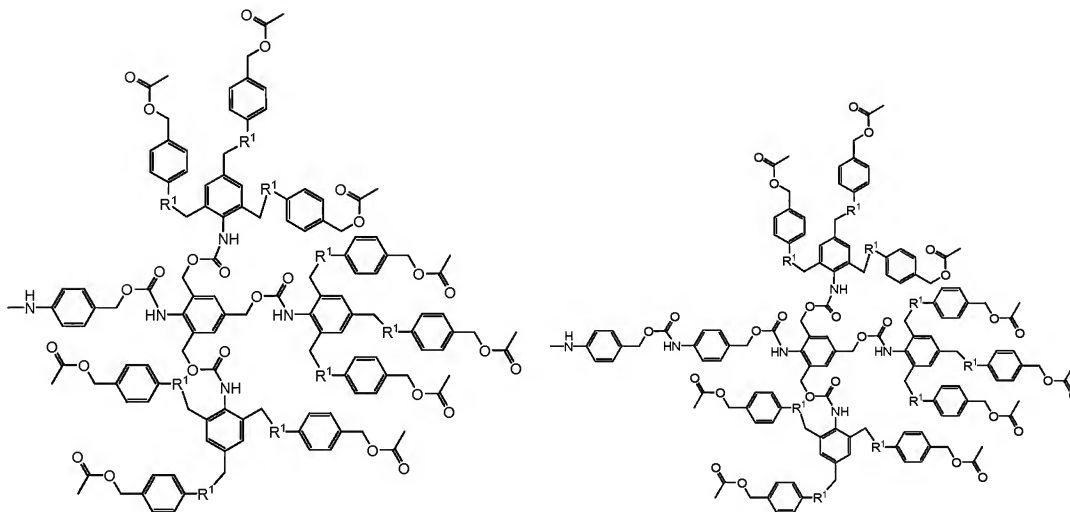
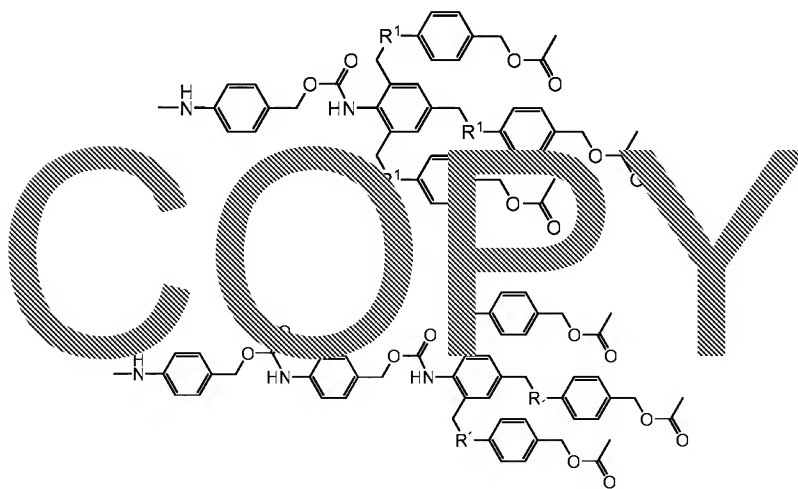
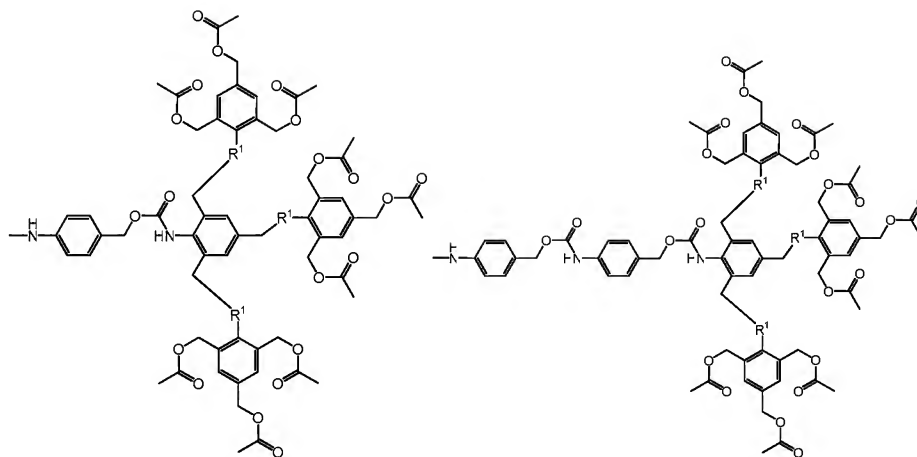
8. (Previously presented) The compound according to claim 4, wherein the **Z** groups are linked to the self-eliminating multiple release spacer or spacer system via an aliphatic N and wherein at least one multiple release spacer or spacer system of either generation **C**, **D** (if present), **E** (if present), or **F** (if present) is a phenol- or thiophenol-based multiple release spacer or spacer system, meaning that

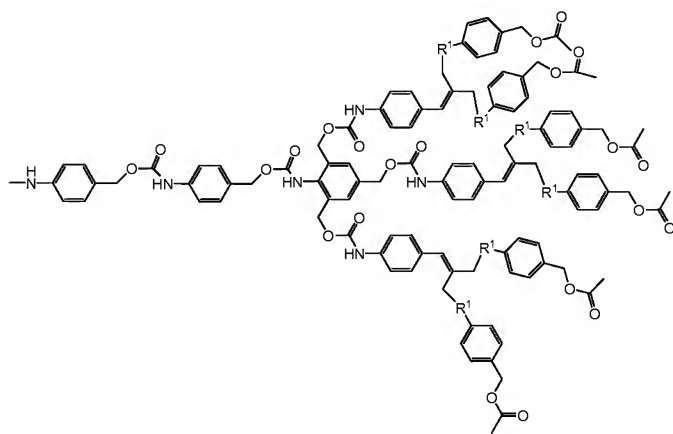
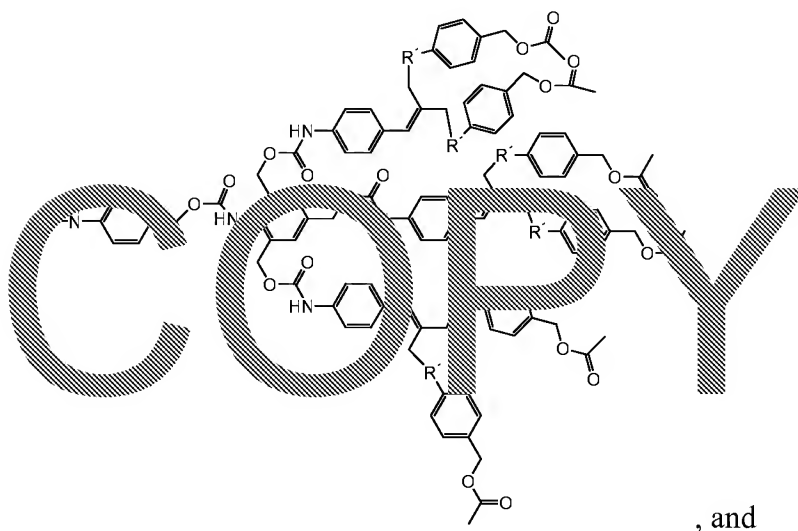
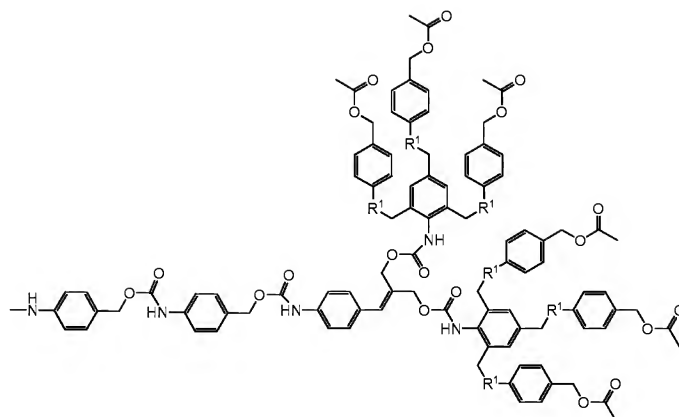
i) **B** = O or S for at least one multiple release spacer in said generation, or

ii) when **B** = N for all multiple release spacers in said generation, at least one single release spacer is connected to at least two branches of at least one multiple release spacer in said generation, and **B** = O or S for at least two of said single release spacers.

9. (Previously presented) The compound according to claim 8, wherein **B** = O or S for all multiple release spacers or spacer systems in said generation.







$R^1 = OC(O)O.$

at least one multiple release spacer or spacer system of either generation **C**, **D** (if present), **E** (if present), or **F** (if present) is a phenol- or thiophenol-based multiple release spacer or spacer system, meaning that

i) **B** = O or S for at least one multiple release spacer in said generation, or

ii) when **B** = N for all multiple release spacers in said generation, at least one single release spacer is connected to at least two branches of at least one multiple release spacer in said generation, and **B** = O or S for at least two of said single release spacers.

24. (Previously presented) The compound according to claim 23, wherein **B** = O or S for all multiple release spacers or spacer systems in said generation.

25. (Previously presented) The compound according to claim 23, wherein the phenol- or thiophenol-based multiple release spacer is connected to either **X** or **Z**.

26-30. (Canceled)

31. (Previously presented) The compound according to claim 4, wherein the specifier **V** is a tripeptide.

32. (Previously presented) The compound according to claim 31, wherein the tripeptide is linked via its C-terminus to the self-eliminating multiple release spacer or spacer system.

33. (Previously presented) The compound of claim 32, wherein the C-terminal amino acid residue of the tripeptide is selected from arginine and lysine, the middle amino acid residue of the tripeptide is selected from alanine, valine, leucine, isoleucine, methionine, phenylalanine, cyclohexylglycine, tryptophan and proline, and the N-terminal amino acid residue of the tripeptide is selected from a D-amino acid residue and a protected L-amino acid residue including protected glycine.

34. (Previously presented) The compound according to claim 33, wherein the specifier **V** is selected from D-alanylphenylalanyllysine, D-valylleucyllysine, D-alanylleucyllysine, D-valylphenylalanyllysine, D-valyltryptophanyllysine and D-alanyltryptophanyllysine.

and salts thereof, wherein  $R^7 = OC(O)O$ .

44. (Canceled)

45. (Previously presented) A diagnostic assay process, the process comprising: incubating a sample comprising an enzyme with a compound according to claim 4 to cause enzymatic cleavage of the compound, and detecting one or more molecules liberated by the enzymatic cleavage.

46. (Previously presented) The diagnostic assay process according to claim 45, wherein the detection of the one or more molecules determines the presence or amount of the enzyme

47. (Previously presented) The diagnostic assay process according to claim 46, wherein the detection of the one or more molecules determines the presence or amount of protease.

48. (Previously presented) The diagnostic assay process according to claim 47, wherein the compound that is used comprises a substrate for said protease and one or more **Z** groups are detected.

49. (Previously presented) The diagnostic assay process according to claim 47, wherein the compound that is used comprises a substrate for the enzyme, which is the product of cleavage of its pro-enzyme precursor by said protease and one or more **Z** groups are detected.

50. (Previously presented) A composite structure comprising two or more compounds according to claim 4 connected with a polymeric structure.

51. (Previously presented) The compound according to claim 4, wherein the specifier **V** can be removed or transformed by an enzyme that is transported to the vicinity of or inside target cells or target tissue via ADEPT, PDEPT, MDEPT, VDEPT, or GDEPT.

52. (Canceled)